Induction of site-specific chromosomal translocations in embryonic stem cells by CRISPR/Cas9.

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Public Summary:
Chromosomal translocation is often associated with congenital genetic disorders, infertility, and cancers. The lack of cellular and animal models for chromosomal translocations, however, has hampered our ability to understand the underlying disease mechanisms and to develop new therapies. In this study, we showed that chromosomal translocations can be generated in mouse embryonic stem cells (ESCs) via CRISPR/Cas9, a new gene editing technology. Mouse ESCs carrying translocated chromosomes can be isolated and expanded to establish stable cell lines. Furthermore, we used these ESCs to generate mice carrying the same chromosome translocation. The establishment of ESC-based cellular and animal models of chromosomal translocation provides a powerful platform for understanding the effect of chromosomal translocation and for the development of new therapeutic strategies.

Scientific Abstract:
Chromosomal translocation is the most common form of chromosomal abnormality and is often associated with congenital genetic disorders, infertility, and cancers. The lack of cellular and animal models for chromosomal translocations, however, has hampered our ability to understand the underlying disease mechanisms and to develop new therapies. Here, we show that site-specific chromosomal translocations can be generated in mouse embryonic stem cells (mESCs) via CRISPR/Cas9. Mouse ESCs carrying translocated chromosomes can be isolated and expanded to establish stable cell lines. Furthermore, chimeric mice can be generated by injecting these mESCs into host blastocysts. The establishment of ESC-based cellular and animal models of chromosomal translocation by CRISPR/Cas9 provides a powerful platform for understanding the effect of chromosomal translocation and for the development of new therapeutic strategies.